drome may lead to elevation of hepatic enzymes. Toxicity is unusual at serum salicylate levels of less than 20 mg per dl, but in one series toxicity occurred in all patients with juvenile rheumatoid arthritis in whom levels were greater than 25 mg per dl. Liver biopsy studies show a mononuclear cell infiltrate of the portal triads with scattered cellular necrosis that occasionally is consistent with chronic active hepatitis. As with acetaminophen, the toxicity is reversible. Lower dosages can be reinstituted providing the hepatic enzymes and serum salicylate level are monitored closely.

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Cimetidine in the Treatment of Peptic Ulcer Disease

A NEW CLASS of compounds, termed the histamine type 2 or H-2 receptor antagonists, has been added to the ever-expanding list of drugs used in the treatment of acid peptic ulcer disease. Cimetidine, the only H-2 antagonist currently available in the United States, has undergone extensive basic research testing and clinical trials documenting its ability to profoundly decrease gastric acid secretion. Histamine receptors on the gastric parietal cell playing an important role in the stimulation of hydrochloric acid secretion through all modalities (cephalic phase by vagal innervation, stimulated by food and stimulated by gastrin) are not antagonized by the traditional antihistamines (called H-1 receptor antagonists) such as diphenhydramine (Benadryl®). The H-2 receptor antagonists, such as cimetidine, block to a major degree the acid output stimulated by all known gastric secretagogues.

Early H-2 receptor antagonists, particularly metiamide, were found in some clinical trials to be associated with neutropenia on rare occasions. However, no significant toxicity has been found with cimetidine use, although isolated reports of gynecomastia have appeared. Cimetidine cannot yet be recommended to pregnant or nursing women.

Cimetidine has been shown to be effective in healing duodenal ulcers. Gastric acid secretion and acid delivery to the duodenum are significantly reduced with cimetidine therapy and it is associated with an improved rate of ulcer healing. Studies are in progress assessing the efficacy of cimetidine therapy in gastritis and gastric ulceration, as well as the prophylactic usefulness of continuous long-term nocturnal cimetidine administration for acid peptic disease.

Cimetidine usage should be considered in patients with gastric acid hypersecretory states such as Zollinger-Ellison syndrome and systemic mastocytosis and in patients who cannot or will not take effective doses of antacids for duodenal ulcer disease. The oral dosage is one 300 mg tablet with each meal and an additional 300 mg at bedtime. A parenterally administered form is available for patients who cannot take orally given medication. The drug should be administered in these latter patients in a dosage of 300 mg (mixed with 100 ml of a 5 percent dextrose solution) every six hours. The drug should not be used for dyspepsia without documented duodenal ulceration and it should be used with caution in patients with routine duodenal ulcers. With this drug, as with all new drugs, practicing physicians must be alert to unusual, unreported manifestations of toxicity.

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Pituitary Cushing Syndrome: New Options for Treatment

HYPERCORTISOLISM in two thirds of all cases is secondary to excessive secretion of adrenocorticotropic hormone (ACTH) by the pituitary gland (pituitary Cushing syndrome). The mainstay of treatment for more than three decades has been total bilateral adrenalectomy. This treatment has brought its own problems including a significant mortality rate, persistent or recurrent hypercortisolism due to hyperplastic remnant or ectopic adrenal tissue, postoperative pituitary tumors (Nelson syndrome) and, almost invariably, lifelong dependence upon replacement therapy with adrenocortical hormones. Recent therapeutic advances now offer promise of making total adrenalectomy obsolete over the next few years.

Pituitary radiation has been used with limited success as a primary treatment in adults, perhaps